09/316313

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=> d his

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                E US2187847/PN
L1             1 S E3

     FILE 'STNGUIDE' ENTERED AT 10:05:06 ON 21 MAR 2002

     FILE 'BEILSTEIN' ENTERED AT 10:08:40 ON 21 MAR 2002
L2             1 S 341102/BRN

     INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
     BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
     DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 10:11:02 ON
     21 MAR 2002
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               0*  FILE USPAT2
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L4             5 S E3
                 SELECT L4 2 RN

     FILE 'REGISTRY' ENTERED AT 10:13:54 ON 21 MAR 2002
L5             4 S E1-E4
L6             1 S L5 AND   C21 H27 N3 O3/MF
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=> d 1-3 fbib abs

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:885621 CAPLUS
DN 136:11188
TI A combination kit used in the treatment of malaria
IN Pinto, Francis Joseph; Piramal, Swati Ajay; **Pratap, Ram**; Bhaduri, Amiya Prasad; Thapliyal, Harsh Pati; Puri, Sunil Kumar; Dutta, Guru Prasad; Dwivedi, Anil Kumar; Singh, Satyawan; Srivastava, Pratima; Pandey, Vikash Chandra; Srivastava, Sudhir; Singh, Shio Kumar; Gupta, Ram Chandra; Srivastava, Jagdishwar Sahai; Asthana, Omkar Prasad
PA Nicholas Piramal India Ltd., India; Council of Scientific and Industrial Research
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001091535 | A2 | 20011206 | WO 2000-IN81 | 20000830 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | | | IN 2000-MU501 | A 20000531 |
| BR 2000005247 | A | 20020213 | BR 2000-5247 | 20001106 |
| | | | IN 2000-MU501 | A 20000531 |

AB A combination kit for the treatment of malaria caused by Plasmodium vivax comprises (i) individual doses of 3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]-dihydro-2(3H)-furanone (I) in the form of capsules, (ii) individual doses of chloroquine in the form of tablets, and (iii) instruction material for the administration of the two antimalarial drugs. The combination kit is particularly suited for a 6 days treatment regimen where the treatment is rendered by 5 tablets contg. 500 mg of chloroquine phosphate (equiv. to 300 mg base), 3 tablets to be taken on Day 1 and 1 tablet each on Days 2 and 3, and 5 capsules contg. 25 mg of I, 1 capsule to be taken on Days 2 to 6.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2000:839054 CAPLUS
DN 134:502
TI Use of a primaquine derivative for the treatment of malaria, and process for its prepn.
IN **Pratap, Ram**; Bhaduri, Amiya Prasad; Thapliyal, Harsh Pati; Puri, Sunil Kumar; Dutta, Guru Prasad; Dwivedi, Anil Kumar; Singh, Satyawan; Srivastava, Pratima; Pandey, Vikash Chandra; Srivastava, Sudhir; Singh, Shio Kumar; Gupta, Ram Chandra; Srivastava, Jagdishwar Sahai; Asthana, Omkar Prasad
PA Council of Scientific and Industrial Research, India
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 1055427 | A1 | 20001129 | EP 2000-302430 | 20000324 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | | | IN 1999-655 | A 19990429 |
| | | | US 1999-316313 | A 19990521 |

AB The invention discloses a novel use of primaquine deriv. N1-(3-ethylidinotetrahydrofuran-2-one)-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine in the treatment and controlling the spread of malaria. In particular, the invention discloses a method of treatment of malaria by the use of primaquine deriv. N1-(3-ethylidinotetrahydrofuran-2-one)-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine as a gametocytocidal agent.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2000:493073 CAPLUS

DN 133:100051
TI Hypolipidemic and hypoglycemic pregnadienes
IN **Pratap, Ram**; Gupta, Ram Chandra; Chander, Ramesh; Khanna, Ashok Kumar; Srivastava, Arvind Kumar; Raina, Deepak; Singh, Satyavan; Srivastava, Savita; Rastogl, Anil Kumar; Asthana, Omkar Prasad; Nityanand, Swarna; Anand, Nitya; Ghatak, Ashim; Kapoor, Narinder Kumar; Dev, Sukh
PA Council of Scientific and Industrial Research, India
SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 1020191 | A1 | 20000719 | EP 1999-302556 | 19990331 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | | | IN 1999-DE67 | A 19990112 |

OS MARPAT 133:100051
AB The invention provides a method of using pregnadienones and pregnadienols. Prepn., hypolipidemic,, hypoglycemic, and anticholesteremic activities in rats of 3.beta.-hydroxypregna-5,16-dien-20-one were given in examples.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> select l4
ENTER ANSWER NUMBER OR RANGE (1-):2
ENTER DISPLAY CODE (TI) OR ?:rn
E1 THROUGH E4 ASSIGNED

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 9.59 | 46.12 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -1.86 | -1.86 |

FILE 'REGISTRY' ENTERED AT 10:13:54 ON 21 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


STRUCTURE FILE UPDATES: 19 MAR 2002 HIGHEST RN 401892-67-9
DICTIONARY FILE UPDATES: 19 MAR 2002 HIGHEST RN 401892-67-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

=> s e1-e4
1 517-23-7/BI
(517-23-7/RN)

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             1 70-18-8/BI
               (70-18-8/RN)
             1 79781-00-3/BI
               (79781-00-3/RN)
             1 90-34-6/BI
               (90-34-6/RN)
L5           4 (517-23-7/BI OR 70-18-8/BI OR 79781-00-3/BI OR 90-34-6/BI)

=> d scan

L5   4 ANSWERS   REGISTRY  COPYRIGHT 2002 ACS
IN   2(3H)-Furanone, 3-acetyldihydro- (8CI, 9CI)
MF   C6 H8 O3
CI   COM
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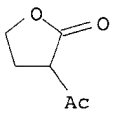


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L5   4 ANSWERS   REGISTRY  COPYRIGHT 2002 ACS
IN   2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-
     quinolinyl)amino]pentyl]amino]ethylidene]- (9CI)
MF   C21 H27 N3 O3
CI   COM
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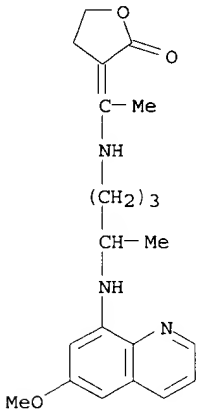


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


L5   4 ANSWERS   REGISTRY  COPYRIGHT 2002 ACS
IN   Glycine, L-.gamma.-glutamyl-L-cysteinyl- (9CI)
MF   C10 H17 N3 O6 S
CI   COM

Absolute stereochemistry.
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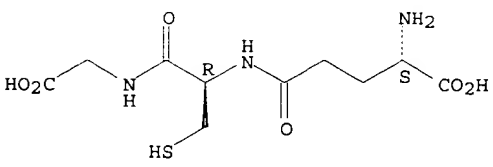

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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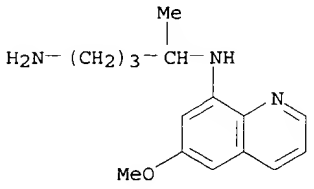
CI COM



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

ALL ANSWERS HAVE BEEN SCANNED

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E US2187847/PN
L1 1 S E3

FILE 'STNGUIDE' ENTERED AT 10:05:06 ON 21 MAR 2002

FILE 'BEILSTEIN' ENTERED AT 10:08:40 ON 21 MAR 2002
L2 1 S 341102/BRN

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 10:11:02 ON 21 MAR 2002

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| 0* FILE ADISINSIGHT |
| 0* FILE ADISNEWS |
| 0* FILE AGRICOLA |
| 0* FILE ANABSTR |
| 0* FILE AQUASCI |
| 0* FILE BIOBUSINESS |
| 0* FILE BIOCOMMERCE |
| 0* FILE BIOSIS |
| 0* FILE BIOTECHABS |
| 0* FILE BIOTECHDS |
| 0* FILE BIOTECHNO |
| 0* FILE CABA |
| 0* FILE CANCERLIT |
| 0* FILE CAPLUS |
| 0* FILE CEABA-VTB |
| 0* FILE CEN |
| 0* FILE CIN |
| 0* FILE CONFSCI |
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| 0* FILE CROPU |
| 0* FILE DDFB |
| 0* FILE DDFU |
| 0* FILE DGENE |
| 0* FILE DRUGB |
| 0* FILE DRUGLAUNCH |
| 0* FILE DRUGMONOG2 |

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                0*  FILE ESBIOBASE
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                0*  FILE FROSTI
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                0*  FILE GENBANK
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                0*  FILE JICST-EPLUS
                0*  FILE KOSMET
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                0*  FILE MEDLINE
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                0*  FILE WPIDS
                0*  FILE WPINDEX
L3               QUE L2
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L4               5 S E3
                  SELECT L4 2 RN

     FILE 'REGISTRY' ENTERED AT 10:13:54 ON 21 MAR 2002
L5               4 S E1-E4

=> s l5 and   C21 H27 N3 O3/mf
            670 C21 H27 N3 O3/MF
L6            1 L5 AND   C21 H27 N3 O3/MF

=> d all

L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   79781-00-3  REGISTRY
CN   2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-
     quinolinyl)amino]pentyl]amino]ethylidene]- (9CI)   (CA INDEX NAME)
OTHER NAMES:
CN   Bulaquine
CN   CDRI 80/53
CN   Compound 80/53
FS   3D CONCORD
DR   223661-25-4
MF   C21 H27 N3 O3
CI   COM
LC   STN Files:   ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, DDFU,
       DRUGU, EMBASE, PHAR, TOXCENTER
         (*File contains numerically searchable property data)

Ring System Data

Elemental|Elemental| Size of |Ring System|    Ring    |    RID
Analysis |Sequence |the Rings|   Formula  |Identifier|Occurrence
   EA    |    ES   |    SZ   |     RF     |    RID   |   Count
=========+=========+=========+============+==========+==========
C4O      |OC4      |5        |C4O         |16.138.1  |1
C5N-C6   |NC5-C6   |6-6      |C9N         |591.79.52 |1
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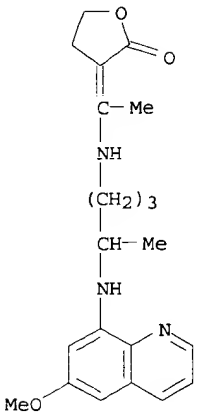

Calculated Properties (CALC)

| CODE | PROPERTY | VALUE | CONDITION | NOTE |
|---|---|---|---|---|
| HD | H donors | 2 | | ACD (1) |
| HAC | H acceptors | 6 | | ACD (1) |
| MW | Molecular Weight | 369.46 | | ACD (1) |
| LOGP | logP | 2.936+/-0.476 | | ACD (1) |
| LOGD | logD | -2.62 | pH 1 | ACD (1) |
| LOGD | logD | -0.92 | pH 4 | ACD (1) |
| LOGD | logD | 2.54 | pH 7 | ACD (1) |
| LOGD | logD | 2.88 | pH 8 | ACD (1) |
| LOGD | logD | 2.94 | pH 10 | ACD (1) |
| PKA | pKa | 7.16+/-0.20 | Most Basic | ACD (1) |
| SLB.MOL | Molar Solubility | >=1 mol/L | pH 1 | ACD (1) |
| SLB.MOL | Molar Solubility | >=0.1 - <1 mol/L | pH 4 | ACD (1) |
| SLB.MOL | Molar Solubility | <0.01 mol/L | pH 7 | ACD (1) |
| SLB.MOL | Molar Solubility | <0.01 mol/L | pH 8 | ACD (1) |
| SLB.MOL | Molar Solubility | <0.01 mol/L | pH 10 | ACD (1) |

(1) Calculated using Advanced Chemistry Development (ACD) Software Solaris V4.67 ((C) 1994-2002 ACD)

22 REFERENCES IN FILE CA (1967 TO DATE)
22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1

AN 136:15004 CA
TI Plasmodium vivax polymorphism in a clinical drug trial
AU Adak, T.; Valecha, Neena; Sharma, V. P.
CS Malaria Research Centre (ICMR), Delhi, 110 054, India
SO Clinical and Diagnostic Laboratory Immunology (2001), 8(5), 891-894
CODEN: CDIMEN; ISSN: 1071-412X
PB American Society for Microbiology
DT Journal
LA English
CC 1-5 (Pharmacology)
AB Data from a double-blind randomized clin. drug trial were analyzed to find the comparative responses of two antirelapse drugs, bulaquine and primaquine, against different relapsing forms of Plasmodium vivax infection. A 1-yr follow-up study strongly suggests that the duration of preerythrocytic development of P. vivax is a polymorphic characteristic, exhibited by two strains of hypnozoites responsible for early and late manifestations after primary infection. Short-term relapses were significantly higher in the first half year than long-term relapses, and the reverse was true in the second half year. Clin. drug response data showed that the hypnozoites characterized for short-term relapse were not susceptible to either of the antirelapse drugs in the currently administered dose, whereas hypnozoites characterized for long incubation were significantly susceptible.
ST bulaquine primaquine antimalarial Plasmodium vivax polymorphism
IT Antimalarials
Genetic polymorphism

Human
Plasmodium vivax
(bulaquine and primaquine against different relapsing forms of Plasmodium vivax infection in humans)

IT 90-34-6, Primaquine 79781-00-3, Bulaquine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bulaquine and primaquine against different relapsing forms of Plasmodium vivax infection in humans)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Adak, T; Am J Trop Med Hyg 1998, V59, P175 MEDLINE
(2) Aliving, A; Am J Trop Med Hyg 1953, V6, P970
(3) Beutler, E; Pharmacol Rev 1969, V21, P73 MEDLINE
(4) Bruce-Chwatt, L; Chemotherapy of malaria, 2nd ed Monograph series no 27 1981
(5) Clyde, D; Am J Trop Med Hyg 1977, V26, P562 MEDLINE
(6) Coatney, G; Am J Hyg 1950, V51, P200
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(8) Cohen, R; N Engl J Med 1968, V279, P1127 MEDLINE
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(11) Joshi, H; Trans R Soc Trop Med Hyg 1977, V91, P231
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(13) Krotoski, W; N Engl J Med 1980, V303, P587 MEDLINE
(14) Lysenko, A; WHO Bull 1977, V55, P541 MEDLINE
(15) Mather, K; Statistical analysis in biology, 4th ed 1951, P1
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(18) Rieckmann, K; Lancet 1989, Vii, P1183
(19) Rosenberg, R; Science 1989, V245, P973 CAPLUS
(20) Roy, R; Ind J Med Res 1979, V69, P939 MEDLINE
(21) Schuurkamp, G; Trans R Soc Trop Med Hyg 1992, V86, P121 MEDLINE
(22) Sharma, M; J Commun Dis 1973, V5, P167
(23) Tarlov, A; Arch Intern Med 1962, V109, P137
(24) Valecha, N; Curr Sci 2001, V80, P561 CAPLUS
(25) Whithy, M; Lancet 1989, Vii, P1389

REFERENCE 2

AN 136:11188 CA
TI A combination kit used in the treatment of malaria
IN Pinto, Francis Joseph; Piramal, Swati Ajay; Pratap, Ram; Bhaduri, Amiya Prasad; Thapliyal, Harsh Pati; Puri, Sunil Kumar; Dutta, Guru Prasad; Dwivedi, Anil Kumar; Singh, Satyawan; Srivastava, Pratima; Pandey, Vikash Chandra; Srivastava, Sudhir; Singh, Shio Kumar; Gupta, Ram Chandra; Srivastava, Jagdishwar Sahai; Asthana, Omkar Prasad
PA Nicholas Piramal India Ltd., India; Council of Scientific and Industrial Research
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
ICI A61
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001091535 | A2 | 20011206 | WO 2000-IN81 | 20000830 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | BR 2000005247 | A | 20020213 | BR 2000-5247 | 20001106 |

PRAI IN 2000-MU501 20000531

AB A combination kit for the treatment of malaria caused by Plasmodium vivax comprises (i) individual doses of 3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]-dihydro-2(3H)-furanone (I) in the form of capsules, (ii) individual doses of chloroquine in the form of tablets, and (iii) instruction material for the administration of the two antimalarial drugs. The combination kit is particularly suited for a 6 days treatment regimen where the treatment is rendered by 5 tablets contg. 500 mg of chloroquine phosphate (equiv. to 300 mg base), 3 tablets to be taken on Day 1 and 1 tablet each on Days 2 and 3, and 5 capsules contg. 25

mg of I, 1 capsule to be taken on Days 2 to 6.
ST primaquine deriv capsule chloroquine tablet antimalarial kit
IT Drug delivery systems
(capsules; combination kit contg. chloroqine and primaquine deriv. used in treatment of malaria)
IT Antimalarials
(combination kit contg. chloroqine and primaquine deriv. used in treatment of malaria)
IT Plasmodium vivax
(infection; combination kit contg. chloroqine and primaquine deriv. used in treatment of malaria)
IT Drug delivery systems
(tablets; combination kit contg. chloroqine and primaquine deriv. used in treatment of malaria)
IT 50-63-5, Chloroquine phosphate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination kit contg. chloroqine and primaquine deriv. used in treatment of malaria)
IT 79781-00-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination kit used in treatment of malaria)
IT 54-05-7, Chloroquine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination kit used in treatment of malaria)

REFERENCE 3

AN 135:189769 CA
TI Comparative antirelapse efficacy of CDRI compound 80/53 (Bulaquine) vs. primaquine in double blind clinical trial
AU Valecha, Neena; Adak, T.; Bagga, A. K.; Asthana, O. P.; Srivastava, J. S.; Joshi, Hema; Sharma, V. P.
CS Malaria Research Centre (ICMR), Delhi, 110 054, India
SO Current Science (2001), 80(4), 561-563
CODEN: CUSCAM; ISSN: 0011-3891
PB Current Science Association
DT Journal
LA English
CC 1-5 (Pharmacology)
AB One-year follow-up of malaria patients was undertaken to monitor the antirelapse efficacy of CDRI compd. 80/53 (Bulaquine). A total of 697 patients of Plasmodium vivax malaria were included in three arm double blind randomized study comparing CDRI 80/53 with placebo and primaquine. Drugs were given once a day for 5 days and the dose for CDRI 80/53 and primaquine was 25 mg and 15 mg, resp. Thirty-four patients were lost to follow-up and 663 patients completed one year trial. Two hundred and fourteen patients came back with second episode during the one-year followup period. A detailed anal. revealed that the relapse rate during non-transmission period with placebo in 16 (10.6%) patients was higher than both in primaquine (3.0%) and CDRI 80/53 (4.9%) groups.
ST Bulaquine primaquine antimalarial Plasmodium
IT Antimalarials
Plasmodium vivax
(comparative antirelapse efficacy of CDRI compd. 80/53 (Bulaquine) vs. primaquine in treatment of malaria in humans)
IT 90-34-6, Primaquine 79781-00-3, Bulaquine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparative antirelapse efficacy of CDRI compd. 80/53 (Bulaquine) vs. primaquine in treatment of malaria in humans)
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Adak, T; Am J Trop Med Hyg 1998, V59, P175 MEDLINE
(2) Anklesaria, P; Tropical Diseases: Molecular Biology and Control Strategies 1994, P256
(3) Anon; CDRI document 1997, 80/53, P50
(4) Chwatt, L; Chemotherapy of Malaria Monograph Series No 27 1986, P61
(5) Desjardins, R; Malaria Principles and Practices of Malariology 1988, V1, P846
(6) Dutta, G; Am J Trop Med Hyg 1989, V41, P635 CAPLUS
(7) Dutta, G; Molecular Biology and Control Strategies 1994, P286
(8) Fletcher, K; Bull WHO 1981, V59, P407 CAPLUS
(9) Gogtay, N; Trans R Soc Trop Med Hyg 1998, V92, P341 MEDLINE
(10) Olliaro, P; Bull WHO 1995, V73, P565 MEDLINE
(11) Peters, W; Ann Trop Med Parasitol 1993, V87, P547 CAPLUS

(12) Puri, S; Am J Trop Med Hyg 1989, V41, P638 CAPLUS
(13) Sharma, R; Epidemiology and Control of Malaria in India 1996, P685
(14) Sharma, R; Epidemiology and Control of Malaria in India 1996, P77 CAPLUS
(15) Sharma, V; J Med Res 1996, V103, P26 MEDLINE
(16) Sinha, S; Indian J Malariol 1989, V26, P83 MEDLINE
(17) WHO Scientific Group; WHO Technical Report Series 1990, 805
(18) Wernsdorfer, W; Primaquine: Pharmacokinetics, Metabolism, Toxicity and Activity 1987

REFERENCE 4

AN 134:502 CA
TI Use of a primaquine derivative for the treatment of malaria, and process for its prepn.
IN Pratap, Ram; Bhaduri, Amiya Prasad; Thapliyal, Harsh Pati; Puri, Sunil Kumar; Dutta, Guru Prasad; Dwivedi, Anil Kumar; Singh, Satyawan; Srivastava, Pratima; Pandey, Vikash Chandra; Srivastava, Sudhir; Singh, Shio Kumar; Gupta, Ram Chandra; Srivastava, Jagdishwar Sahai; Asthana, Omkar Prasad
PA Council of Scientific and Industrial Research, India
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-4706
ICS A61P033-06
CC 1-5 (Pharmacology)
Section cross-reference(s): 27, 63
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 1055427 | A1 | 20001129 | EP 2000-302430 | 20000324 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI IN 1999-655 | | 19990429 | | |
| US 1999-316313 | | 19990521 | | |

AB The invention discloses a novel use of primaquine deriv. N1-(3-ethylidinotetrahydrofuran-2-one)-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine in the treatment and controlling the spread of malaria. In particular, the invention discloses a method of treatment of malaria by the use of primaquine deriv. N1-(3-ethylidinotetrahydrofuran-2-one)-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine as a gametocytocidal agent.

ST primaquine deriv prepn gametocytocidal malaria treatment
IT Drugs
(amino, delivery; primaquine deriv. for treatment of malaria, and prepn. process)
IT Erythrocyte
(glutathione level; primaquine deriv. for treatment of malaria, and prepn. process)
IT Development, microbial
(oocyst; primaquine deriv. for treatment of malaria, and prepn. process)
IT Antimalarials
Drug delivery systems
Drug metabolism
Liver
Plasmodium cynomolgi
(primaquine deriv. for treatment of malaria, and prepn. process)
IT Hemoglobins, methemoglobins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(primaquine deriv. for treatment of malaria, and prepn. process)
IT Development, microbial
(sporozoite; primaquine deriv. for treatment of malaria, and prepn. process)
IT 79781-00-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(primaquine deriv. for treatment of malaria, and prepn. process)
IT 70-18-8, Glutathione, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(primaquine deriv. for treatment of malaria, and prepn. process)
IT 90-34-6, Primaquine 517-23-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; primaquine deriv. for treatment of malaria, and prepn. process)

09/316313

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Olliaro, P; BULLETIN OF THE WORLD HEALTH ORGANIZATION 1995, V73/5, P565
(2) Paliwal, J; JOURNAL OF CHROMATOGRAPHY 1993, V616(1), P155 CAPLUS
(3) Saxena, N; INDIAN JOURNAL OF MEDICAL RESEARCH - SECTION A INFECTIOUS DISEASES 1989, P330 MEDLINE

REFERENCE 5

AN 132:317655 CA
TI A Simple and Rapid Evaluation of Methemoglobin Toxicity of 8-Aminoquinolines and Related Compounds
AU Srivastava, Pratima; Singh, S.; Jain, G. K.; Puri, S. K.; Pandey, V. C.
CS Division of Biochemistry, Central Drug Research Institute, Lucknow, India
SO Ecotoxicol. Environ. Saf. (2000), 45(3), 236-239
CODEN: EESADV; ISSN: 0147-6513
PB Academic Press
DT Journal
LA English
CC 1-5 (Pharmacology)
AB MetHb, a toxic ferric form of Hb, is continuously formed in normal erythrocytes, but during abnormal situations in situ, the level is enhanced. Antimalarial 8-amino-quinolines and related compds. are causative agents for metHb formation. Employing oxyHb, metHb toxicity was about six times higher with primaquine compared to CDRI Compd. 80/53 at 10-9 M concn. MetHb reductase activity was also completely inhibited by primaquine, whereas 24% inhibition was noted in the case of 80/53 at the same concns. Mastomys, a rodent animal model, was found to be equally good for comparative evaluation of metHb toxicity. Further, with the use of primaquine transdermal tape on the Mastomys model, a rise in metHb occurred with increase in time. In conclusion, the study presents simple, economical, less time-consuming methods for the evaluation of metHb toxicity, in vitro and in vivo, without employing the conventional Beagle dog model. (c) 2000 Academic Press.
ST antimalarial aminoquinoline hemotoxicity metHb Mastomys erythrocyte
IT Antimalarials
Erythrocyte
(simple and rapid evaluation of metHb toxicity of antimalarial aminoquinolines and related compds.)
IT Hemoglobins
Hemoglobins, oxyhemoglobins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(simple and rapid evaluation of metHb toxicity of antimalarial aminoquinolines and related compds.)
IT Hemoglobins, methemoglobins
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(simple and rapid evaluation of metHb toxicity of antimalarial aminoquinolines and related compds.)
IT Mastomys
(simple and rapid evaluation of metHb toxicity of antimalarial aminoquinolines and related compds. using Mastomys)
IT 54-05-7, Chloroquine 90-34-6, Primaquine 63968-64-9, Artemisinin 79781-00-3, Compound 80/53
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simple and rapid evaluation of metHb toxicity of antimalarial aminoquinolines and related compds.)
IT 9032-80-8, Methemoglobin reductase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(simple and rapid evaluation of metHb toxicity of antimalarial aminoquinolines and related compds.)
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Clyde, D; Bull World Health Org 1981, V59, P463
(2) Drabkin, D; Am J Physiol 1949, V217, P710 CAPLUS
(3) Evelyn, K; J Biol Chem 1938, V126, P655 CAPLUS
(4) Hegesh, E; J Lab Clin Med 1969, V72, P339
(5) Hsiech, H; The Red Blood Cell 1975, P799
(6) Link, C; Toxicol Appl Pharmacol 1988, V81, P192
(7) Puri, S; Tropen Med Parasitol 1989, V40, P409 MEDLINE
(8) Saxena, N; Clin Chem Enzym Commun 1989, V2, P55
(9) Singh, S; Tropical Diseases, Molecular Biology and Control Strategies 1994, P245 CAPLUS
(10) Srivastava, P; Biochem Pharmacol 1992, V43, P904 CAPLUS
(11) Srivastava, P; Biochem Pharmacol 1993, V46, P1859 CAPLUS

REFERENCE 6

AN 132:170961 CA

09/316313

TI Effect of cyclodextrins on the stability of new antimalarial compound N1-[3'-acetyl-4',5'-dihydro-2'-furanyl]-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine
AU Dwivedi, A. K.; Kulkarni, D.; Khanna, M.; Singh, S.
CS Division of Pharmaceutics, C.D.R.I., Lucknow, 226 001, India
SO Indian J. Pharm. Sci. (1999), 61(3), 175-177
CODEN: IJSIDW; ISSN: 0250-474X
PB Indian Pharmaceutical Association
DT Journal
LA English
CC 63-6 (Pharmaceuticals)
AB CDRI 80/53 (I), the title antimalarial compd., is now under phase II clin. trials. It was obsd. that I is not stable in acidic medium. Therefore, the present investigation was taken up to study the effect of .beta.- and .gamma.-cyclodextrins on the stability of I. The soln. of I as well as its cyclodextrin complexes were prepd. in acetate buffers of different pH values. The order of reaction and degrdn. rate const. at 30.degree. were computed by least-squares linear regression. The I-.beta.-cyclodextrin (1:2) complex showed the best stability of I.
ST cyclodextrin CDRI 8053 complex prepn; antimalarial CDRI 8053 cyclodextrin complex; quinoline dihydrofuran pentanediamine complex cyclodextrin prepn
IT 7585-39-9, .beta.-Cyclodextrin 17465-86-0, .gamma.-Cyclodextrin 79781-00-3, CDRI 80/53
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclodextrins effect on stability of antimalarial CDRI 80/53)
IT 258833-88-4P 258833-89-5P 258833-90-8P 258833-91-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclodextrins effect on stability of antimalarial CDRI 80/53)
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Bhat, B; IN 15811 1983 CAPLUS
(2) Bhat, B; Indian J Chem 1985, V24B, P419 CAPLUS
(3) Dutta, G; Am J Trop Med Hyg 1989, V41, P635 CAPLUS
(4) Dwivedi, A; Indian J Pharm Sci 1997, V59, P321 CAPLUS
(5) Irwin, W; Kinetics of Drug Decomposition, Basic computer solutions 1990, P2
(6) Jain, G; Indian J Pharm Sci 1990, V52, P195 CAPLUS
(7) Loftsson, T; J Pharm Sci 1996, V85, P1022
(8) Monif, T; Indian J Pharm Sci 1993, V55, P196 CAPLUS
(9) Puri, S; Am J Trop Med Hyg 1989, V41, P638 CAPLUS
(10) Seth, R; The Eastern Pharmacist 1989, V32, P123
(11) Sinha, N; Tropical diseases molecular biology control and strategies, Publication & Information directorate 1994, P262

REFERENCE 7

AN 129:211185 CA
TI A rapid and sensitive high performance liquid chromatographic assay of the new antimalarial compound 80/53 in serum with a novel sample clean-up method and its pharmacokinetics in rabbits
AU Paliwal, Jyoti Kumar; Gupta, Ram Chandra
CS Pharnmacokinetics and Metabolism Division, Central Drug Research Institute, Lucknow, 26001, India
SO J. Pharm. Biomed. Anal. (1998), 17(4,5), 775-783
CODEN: JPBADA; ISSN: 0731-7085
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB The compd. 80/53 (AM) is a new antimalarial agent synthesized by this institute as a safer and less toxic analog of primaquine. It was found to exhibit fluorescence in acetonitrile soln. and this finding was exploited to develop a selective and sensitive high performance liq. chromatog. (HPLC) assay of the AM in rabbit serum. The sample clean-up was done in a single step by simultaneous protein pptn. and extn. with acetonitrile in the presence of sodium sulfate. The lower limit of quantitation of the method was 50 ng ml-1 using 100 .mu.l of serum sample. The method was fully validated from 50 to 1600 ng ml-1 concn. range with a recovery ranging from 70 to 75%. The within- and between-run variability was less than 10% and the drug in serum was stable over four freeze-thaw cycles and up to 24 h in injection solvent at 4.degree.C. The method was applied to det. the pharmacokinetic parameters of AM in 5 rabbits receiving a single bolus i.v. and peroral dose in a crossover study. The concn.-time data after a 5 mg kg-1 i.v. dose in rabbits was best fitted to the two compartment body model with first order absorption and elimination rate consts. The terminal half-life and MRT of AM were 95.3 .+-. 43.5 and 104 .+-. 10.6 min resp. After administering a single 20 mg kg-1 oral dose, the serum levels of AM in all the rabbits declined below the quantitation

limit by 90 min and it was not possible to fit the data by the compartmental approach. The MRT of AM after oral dose was 31.1 .+-. 8.3 min. Application of the assay has also been extended to analyze the serum samples of rats, monkeys and humans.

ST antimalarial compd 8053 detn HPLC

IT Blood analysis
(antimalarial compd. 80/53 detn. in blood by HPLC with novel sample clean-up method)

IT Sample preparation
(clean-up method; antimalarial compd. 80/53 detn. in blood by HPLC with novel sample clean-up method)

IT 79781-00-3, Compound 80/53
RL: ANT (Analyte); ANST (Analytical study)
(antimalarial compd. 80/53 detn. in blood by HPLC with novel sample clean-up method)

REFERENCE 8

AN 128:184740 CA

TI Simultaneous determination of a new antimalarial agent, CDRI compound no 80/53 and primaquine by TLC densitometry and UV spectrophotometry

AU Dwivedi, A. K.; Khanna, M.; Pal, R.; Singh, S.

CS Divn. of Pharmaceutics, CDRI, Lucknow, 226 001, India

SO Indian J. Pharm. Sci. (1997), 59(6), 321-323
CODEN: IJSIDW; ISSN: 0250-474X

PB Indian Pharmaceutical Association

DT Journal

LA English

CC 64-3 (Pharmaceutical Analysis)
Section cross-reference(s): 63

AB Compd. 80/53 is a new antimalarial agent developed in a research lab. (CDRI) in India. It is unstable in acidic conditions where it is converted into primaquine. To conduct stability studies of this compd., TLC densitometric and UV spectrophotometric detn. methods were developed. These methods are also suitable for the detn. of 80/53 or primaquine in bulk and pharmaceutical dosage forms.

ST CDRI 8053 detn UV spectrophotometry; primaquine detn UV spectrophotometry

IT 90-34-6, Primaquine 79781-00-3
RL: ANT (Analyte); ANST (Analytical study)
(detn. of 80/53 and primaquine by TLC densitometry and UV spectrophotometry)

REFERENCE 9

AN 123:132069 CA

TI Long term toxicity studies with a synthetic anti-relapse antimalarial compound 80/53 in rats and monkeys

AU Sethi, N.; Srivastava, S.; Singh, R. K.; Puri, S. K.

CS Division of Toxicology, Central Drug Research Institute, Lucknow, 226001, India

SO Indian J. Parasitol. (1993), 17(1), 15-26
CODEN: IJPAES; ISSN: 0253-7168

DT Journal

LA English

CC 1-5 (Pharmacology)

AB The effect of prolonged oral administration of aq. soln. of a new synthetic anti-relapse compd. 80/53, was carried out in rats and monkeys. None of the toxicity parameters in test animals revealed any significant change as compared to control animals. Therefore, it is concluded that the compd. is non-toxic to rodents and non-rodents and thus has been cleared for clin. pharmacol. studies in normal human volunteers.

ST antimalarial compd 8053 toxicity

IT Antimalarials
(toxicity studies with antimalarial compd. 80/53)

IT 79781-00-3, CDRI 80/53
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity studies with antimalarial compd. 80/53)

REFERENCE 10

AN 120:116609 CA

TI Effect of pH on the stability of new antimalarial compound (80/53) N'-3'-acetyl-4',5'-dihydro-2'-furanyl-N4-(6-methoxy-8-quinolinyl)-1,4-pentane diamine

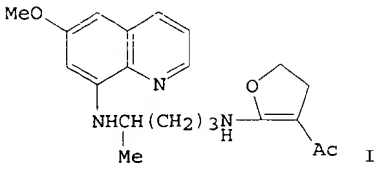
AU Monif, T.; Prakash, P.; Dwivedi, A. K.; Kulkarni, D.; Sarin, J. P. S.

CS Div. Pharm., Cent. Drug Res. Inst., Lucknow, 226 001, India

SO Indian J. Pharm. Sci. (1993), 55(5), 196-7
CODEN: IJSIDW; ISSN: 0250-474X

09/316313

DT Journal
LA English
CC 63-5 (Pharmaceuticals)
GI



I

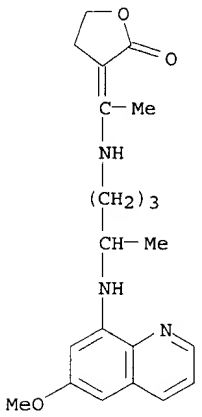
AB A study was conducted to det. the effect of pH on antimalarial compd. 80/53 (I). Aq. solns. of I were prepd. in buffers of different pH values (2.2 to 8.6) at 25.degree.. The order of reaction and degrdn. rate const. were computed by least square linear regression.

ST quinoline deriv antimicrobial stability pH; compd 8053 antimicrobial stability pH

IT 79781-00-3, Compound 80/53
RL: PRP (Properties)
(stability of, in solns., pH effect on)

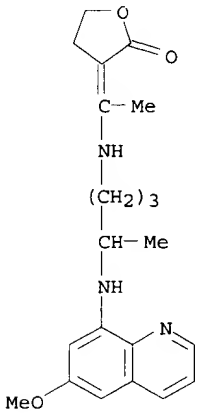
=> d 11-22 fbib abs hitstr

L7 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1994:94848 CAPLUS
DN 120:94848
TI Effect of the antimalarial agents primaquine and CDRI 80/53 [(N'-3-acetyl-4,5-dihydro-2-furanyl)-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine on oxidative stress and antioxidant defenses in mice
AU Srivastava, Pratima; Puri, S. K.; Dutta, G. P.; Pandey, V. C.
CS Div. Biochem. Microbiol., Cent. Drug Res. Inst., Lucknow, 226 001, India
SO Biochem. Pharmacol. (1993), 46(10), 1859-60
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
AB The effects of the newly developed antimalarial compd. CDRI 80/53 and primaquine (PQ) on the antioxidant system of mice were detd. at equieffective antimalarial doses on enzyme systems responsible for protection against O, i.e., hepatic superoxide dismutase and catalase. While PQ inhibited these liver enzyme activities, as detd. in vitro after in vivo administration of the drugs, CDRI 80/53 did not. However, both CDRI 80/53 and PQ increased the level of superoxide anion and lipid peroxidn. It is concluded that CDRI 80/53 has less effect on antioxidant defense enzymes than PQ.
IT **79781-00-3**, CDRI 80/53
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antioxidant defense system of liver response to)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)

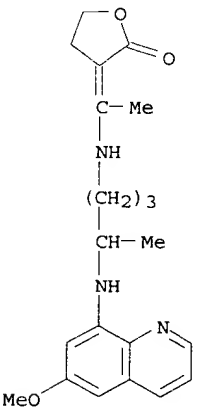


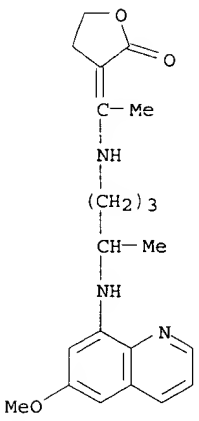

L7 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1994:49934 CAPLUS
DN 120:49934
TI 8-Aminoquinolines effective against Pneumocystis carinii in vitro and in vivo
AU Queener, S. F.; Bartlett, M. S.; Nasr, M.; Smith, J. W.
CS Sch. Med., Indiana Univ., Indianapolis, IN, 46202-5120, USA
SO Antimicrob. Agents Chemother. (1993), 37(10), 2166-72
CODEN: AMACCQ; ISSN: 0066-4804
DT Journal
LA English
AB The activities of 25 8-aminoquinolines were compared in tests assessing the ability of the compds. to inhibit the growth of Pneumocystis carinii in culture. Six compds. were effective at or below 0.03 .mu.M: CDRI 80/53, NSC19894, NSC305805, NSC305812, WR182234, and primaquine. Four others were effective at between 0.2 and 0.03 .mu.M: NSC305835, WR225448, WR238605, and WR242511. Fourteen drugs were also tested in a std. model of P. carinii pneumonia in rats at daily doses of 2 mg/kg of body wt. in drinking water. CDRI 80/53, NSC305805, NSC305835, and WR225448 were extremely effective in the animal model. The effectiveness of WR238605, WR242511, and primaquine in the rat model has been reported elsewhere (Bartlett, M. S., et al., 1991). The length of the alkyl chain sepg. the nitrogens in the substituent at position 8 of the quinoline ring was a strong determinant of anti-P. carinii activity.
IT **79781-00-3**, CDRI 80/53

RL: BIOL (Biological study)
(pneumocystis carinii inhibition by, structure in relation to)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)

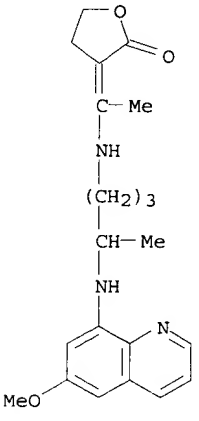


L7 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1993:508314 CAPLUS
DN 119:108314
TI Simultaneous determination of a new antimalarial agent, CDRI compound 80/53, and its metabolite primaquine in serum by high-performance liquid chromatography
AU Paliwal, Jyoti Kumar; Gupta, Ram Chandra; Grover, Pyara Krishen
CS Pharmacokinet. Metab. Div., Cent. Drug Res. Inst., Lucknow, 226001, India
SO J. Chromatogr., Biomed. Appl. (1993), 616(1), 155-60
CODEN: JCBADL; ISSN: 0378-4347
DT Journal
LA English
AB Compd. 80/53 (I) is unstable in acidic conditions where it is converted into primaquine. HPLC assay conditions were optimized to minimize the conversion of I into primaquine. The unchanged I and primaquine were extd. from blood serum samples with hexane/2-propanol (pH > 8). Sepn. was accomplished on a reversed-phase C18 column with acetonitrile-tetrahydrofuran-phosphate buffer as a mobile phase and UV detection at 269 nm. The recoveries of I and primaquine were >70%. No interference was obsd. in exts. from drug-free serum. The detector response was linear with concns. of I and the metabolite in the ranges 25-400 and 10-180 ng/mL, resp., and the within-day coeff. of variation remained at <13.7% for I and <12.5% for primaquine. The method is suitable for the detn. of concn.-time profiles of I and primaquine in human blood serum.
IT **79781-00-3**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in blood serum of human, by HPLC)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)





L7 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1993:32591 CAPLUS
DN 118:32591
TI Sister chromatid exchange and chromosome aberrations analyses for a new 8-aminoquinoline derivative after in vivo exposure in mice
AU Giri, Ashok Kumar; Khan, Kaleem Ahmad; Srivastava, Sushil Kumar; Sethi, Nirmal
CS Div. Toxicol., Cent. Drug Res. Inst., Lucknow, 226 001, India
SO Cytologia (1992), 57(3), 331-4
CODEN: CYTOAN; ISSN: 0011-4545
DT Journal
LA English
AB The present study indicates that the antimalarial compd. 80/53 was not genotoxic in vivo in bone marrow cells of mice.
IT **79781-00-3**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(genotoxicity of)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



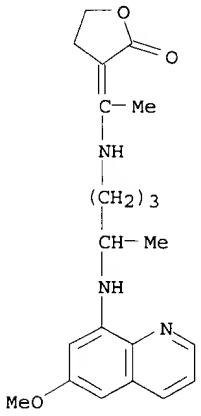
L7 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1992:187567 CAPLUS
DN 116:187567
TI Kinetic and substrate binding characterization of hepatic mixed function oxidase system in monkeys with primaquine and (N1-3-acetyl-4,5-dihydro-2-furanyl)-N4-(methoxy-8-quinolinyl) 1,4-peptanediamine
AU Srivastava, Pratima; Sahni, Sanjeev K.; Tripathi, Lalit M.; Puri, Sunil K.; Dutta, Guru P.; Pandey, Vikash C.
CS Div. Biochem. Microbiol., Cent. Drug Res. Inst., Lucknow, 226 001, India
SO Biochem. Pharmacol. (1992), 43(4), 904-7
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
AB When tested in vitro, primaquine and N1-3-acetyl-4,5-dihydro-2-furanyl)-N4-

(methoxy-8-quinolinyl) 1,4-peptane-diamine (compd. 80/53) (I) inhibited the activities of aniline hydroxylase and aminopyrine-N-demethylase in a concn.-dependent manner. For aniline hydroxylase, the inhibition was non-competitive, whereas for aminopyrine-N-demethylase, the inhibition was competitive. I and primaquine inhibited the binding capacity of cytochrome P 450. Thus, I appears to interfere less with the drug-metabolizing enzymes than primaquine.

IT **79781-00-3**, Compound 80/53
RL: BIOL (Biological study)
(mixed function oxidase of liver inhibition by, kinetics of)

RN 79781-00-3 CAPLUS

CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



L7 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2002 ACS

AN 1991:549680 CAPLUS

DN 115:149680

TI In vitro absorption studies of a new antimalarial in the gastro-intestinal tract

AU Jain, G. K.; Singh, S.

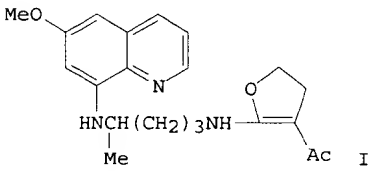
CS Div. Pharm., Cent. Drug Res. Inst., Lucknow, India

SO Indian J. Pharm. Sci. (1990), 52(4), 195-7
CODEN: IJSIDW; ISSN: 0250-474X

DT Journal

LA English

GI

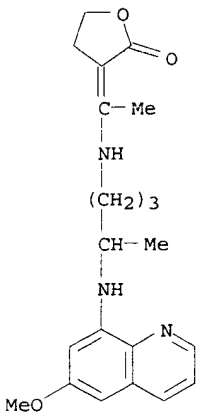


AB CDRI 80/53 (I) is a new antimalarial primaquine deriv. Its in vitro diffusion and absorption rate consts. in the gastrointestinal trace were detd. using a sartonis absorption simulator to model behavior in body fluids. The diffusion rate and absorption rate consts. were 2.9976 .times. 10-4 and 11.70 .times. 10-4, resp. I was rapidly converted to primaquine, the biol. active compd., under acidic pH. .alpha.-Acetyl-.gamma.-butyrolactone liberated during acid treatment may contribute to lower severity of side-effects.

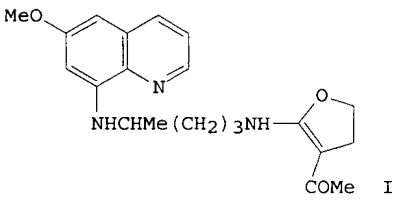
IT **79781-00-3**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, in simulated digestive tract fluids)

RN 79781-00-3 CAPLUS

CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)

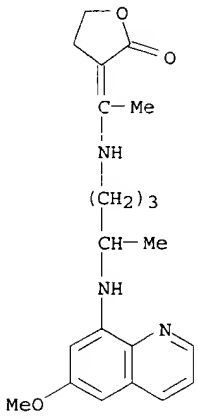


L7 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1991:400261 CAPLUS
DN 115:261
TI Effect of anti-relapse antimalarial compound CDRI 80/53 and primaquine on hepatic mixed function oxidase system of rhesus monkey
AU Pandey, V. C.; Puri, S. K.; Sahni, S. K.; Srivastava, P.; Dutta, G. P.
CS Div. Biochem., Cent. Drug Res. Inst., Lucknow, 226001, India
SO Pharmacol. Res. (1990), 22(6), 701-7
CODEN: PHMREP; ISSN: 1043-6618
DT Journal
LA English
GI

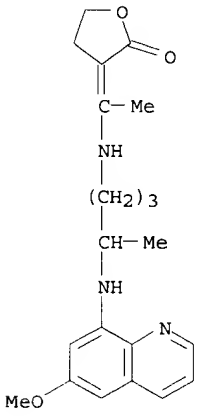


I

AB A potential anti-relapse antimalarial compd. CDRI 80/53 (I) at 7.5 mg/kg body wt. and primaquine at 6.0 mg/kg body wt. did not cause any significant change in the status of hepatic microsomal mixed function oxidase system of rhesus monkeys, when given orally for 7 days. Further, the extension of the treatment at the same dossier up to 21 days resulted in impairment of the different indexes of the MFO system. I inhibited cytochrome P 450, aminopyrine-N-demethylase, aniline and benzo(a)pyrene hydroxylases, cytochrome b5 and heme levels by 17, 11, 58, 0, 36 and 35% whereas the inhibition caused by primaquine was 34, 40, 72, 54, 39 and 38% resp., establishing that the cytochrome P 450 dependent mono-oxygenase system of monkey liver was comparatively less suppressed by I. The cessation of the compd./drug treatment resulted in almost complete reversal of all the MFO activity to normal in a period of about 6 wk.
IT **79781-00-3**, CDRI 80/53
RL: BIOL (Biological study)
(hepatic mixed function oxidase system response to)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



L7 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1990:417511 CAPLUS
DN 113:17511
TI Pharmacology of compound CDRI 80/53; a potential new antirelapse antimalarial agent
AU Kar, K.; Patnaik, G. K.; Puri, S. K.; Dutta, G. P.
CS Div. Pharmacol., Cent. Drug Res. Inst., Lucknow, 226001, India
SO Indian J. Parasitol. (1988), 12(2), 259-62
CODEN: IJPAES; ISSN: 0253-7168
DT Journal
LA English
AB Pharmacol. of CDRI 80/53, a potential antirelapse antimalarial, was studied in mice and rats. The compd. is devoid of any marked systemic pharmacol. effects in these species. The LD50 values indicate that CDRI 80/53 is less toxic than primaquine. The toxicity, behavioral, analgesic, anticonvulsant, blood pressure, respiration, ECG, anti-inflammatory, and diuretic effects data are presented.
IT **79781-00-3**, CDRI 80/53
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pharmacol. and toxicity of)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



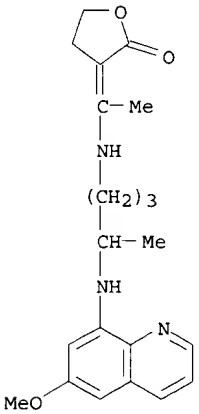
L7 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1990:171805 CAPLUS
DN 112:171805
TI Methemoglobin toxicity and hematological studies on malaria anti-relapse compound CDRI 80/53 in dogs
AU Puri, S. K.; Srivastava, Rahul; Pandey, V. C.; Sethi, N.; Dutta, G. P.
CS Div. Microbiol., Biochem., Toxicol., Cent. Drug Res. Inst., Lucknow, India
SO Am. J. Trop. Med. Hyg. (1989), 41(6), 638-42
CODEN: AJTHAB; ISSN: 0002-9637
DT Journal
LA English

AB MetHb toxicities of primaquine and N1-(3-acetyl-4,5-dihydro-2-furanyl)-N4-(6-methoxy-8-quinolinyl)-1,4-pentanediamine, CDRI 80/53, were compared in beagles. Primaquine administration at 3 mg/kg for 7 days produced high methemoglobinemia and the levels increased 10.55-fold. Compd. 80/53 at 3.75 mg/kg for 7 days produced a marginal increase in methemoglobinemia (3.24-fold). The metHb formed after primaquine administration was 3.65-fold higher than that formed after administration of compd. 80/53. There was no significant change in other hematol. parameters and liver function tests.

IT **79781-00-3**, CDRI 80/53
RL: PRP (Properties)
(toxicity of, to blood and liver, methemoglobinemia in relation to)

RN 79781-00-3 CAPLUS

CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



L7 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2002 ACS

AN 1990:151300 CAPLUS

DN 112:151300

TI Radical curative activity of a new 8-aminoquinoline derivative (CDRI 80/53) against Plasmodium cynomolgi B in monkeys

AU Dutta, G. P.; Puri, S. K.; Bhaduri, A. P.; Seth, Manju

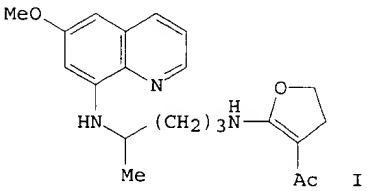
CS Div. Microbiol. Med. Chem., Cent. Drug Res. Inst., Lucknow, India

SO Am. J. Trop. Med. Hyg. (1989), 41(6), 635-7
CODEN: AJTHAB; ISSN: 0002-9637

DT Journal

LA English

GI



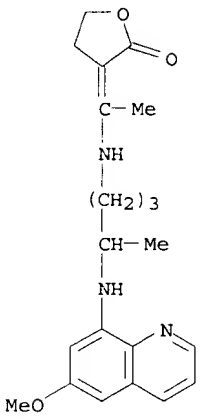
I

AB An analog of primaquine, N1-(3-acetyl-4,5-dihydro-2-furanyl)-N4-(6-methoxy-8-quinolinyl) 1,4-pentanediamine, CDRI Code 80/53) I was evaluated for anti-relapse activity against sporozoite induced P. cynomolgi B infection in rhesus monkeys. The compd. has shown 100% curative anti-relapse activity at 1.25 mg/kg .times. 7 day dose schedule, thereby giving a primaquine index of 0.8.

IT **79781-00-3**, CDRI 80/53
RL: BIOL (Biological study)
(Plasmodium cynomolgi infection response to)

RN 79781-00-3 CAPLUS

CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



L7 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1987:477648 CAPLUS
DN 107:77648
TI Preparation of 8-[[4-[(3-alkanoyl-4,5-dihydro-2-furanyl)amino]-1-methylbutyl]amino]-6-methoxyquinolines as antimalarials
IN Bhat, Balkrishan; Seth, Manju; Bhaduri, Amiya Prashad; Raina, Rita; Pal, Nandlal; Chandra, Subhash; Sen, Amiya Bhushan
PA Council of Scientific and Industrial Research (India), India
SO Indian, 11 pp.
CODEN: INXXAP
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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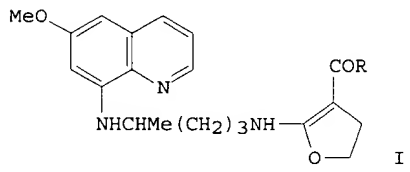
| IN 158111 | A | 19860906 | IN 1982-DE389 | 19820524 |

GI



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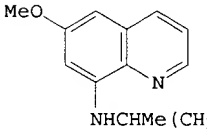
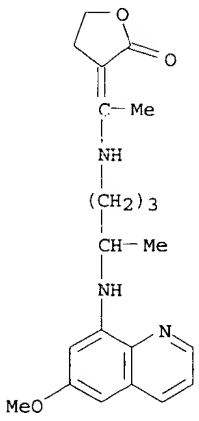
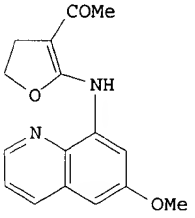


II

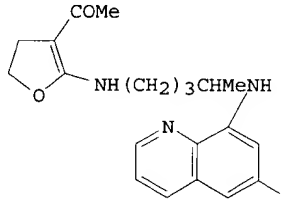
AB The title compds. (I; R = alkyl) were prepd. as antimalarials (no data). [(Aminobutyl)amino]quinoline II (salt anion X unspecified) was refluxed 30 min with 2-acetylbutyrolactone in EtOH contg. Et3N to give 65% I (R = Me).
IT **79781-00-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antimalarial)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)



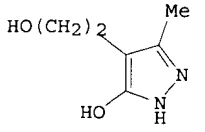
L7 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1981:602870 CAPLUS
DN 95:202870
TI Reaction of .alpha.-acetylbutyrolactone with amines and hydrazine
AU Bhat, Balkrishen; Seth, M.; Bhaduri, A. P.
CS Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226 001, India
SO Indian J. Chem., Sect. B (1981), 20B(8), 703-5
CODEN: IJSBDB; ISSN: 0376-4699
DT Journal
LA English
GI



II



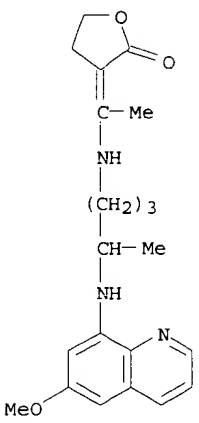
III



IV

AB Reaction of .alpha.-acetylbutyrolactone (I) with 8-amino-6-methoxyquinoline or with 6-methoxy-8-[(1-methyl-4-aminobutyl)amino]quinoline gave II and III, resp. On the other hand, reaction of I with N2H4 gave IV.

IT **79781-00-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 79781-00-3 CAPLUS
CN 2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-quinolinyl)amino]pentyl]amino]ethylidene]- (9CI) (CA INDEX NAME)


O
O
C— Me
NH
(CH2)3
CH— Me
NH
N
MeO

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=> s e3
L1            1 "COMPOUND 80/53"/CN

=> d

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   79781-00-3  REGISTRY
CN   2(3H)-Furanone, dihydro-3-[1-[[4-[(6-methoxy-8-
     quinolinyl)amino]pentyl]amino]ethylidene]-  (9CI)   (CA INDEX NAME)
OTHER NAMES:
CN   Bulaquine
CN   CDRI 80/53
CN   Compound 80/53
FS   3D CONCORD
DR   223661-25-4
MF   C21 H27 N3 O3
CI   COM
LC   STN Files:   ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, DDFU,
       DRUGU, EMBASE, PHAR, TOXCENTER
         (*File contains numerically searchable property data)
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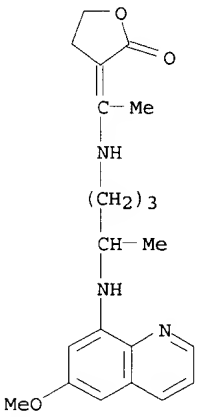


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              22 REFERENCES IN FILE CA (1967 TO DATE)
              22 REFERENCES IN FILE CAPLUS (1967 TO DATE)
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